Aiding the diagnosis of dissociative identity disorder: A pattern recognition study of brain biomarkers

Antje A.T. S. Reinders, PhD [1,2§^], Andre F. Marquand, PhD [3,4^],
Yolanda R. Schlumpf, PhD [5,6*], Sima Chalavi, PhD [2,7*],
Eline M. Vissia, PhD [2,8], Ellert R.S. Nijenhuis, PhD [6], Paola Dazzan, PhD [9],
Lutz Jäncke, PhD [6,10], Dick J. Veltman, PhD [11]

[1] Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London SE5 8AF, United Kingdom

[2] Department of Neuroscience, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands

[3] Donders institute for Brain Cognition and Behaviour, Radboud University, Nijmegen, the Netherlands.

[4] Department of Clinical Neuroscience, Centre for Neuroimaging Sciences, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK

[5] Division of Neuropsychology, Department of Psychology, University of Zurich, Switzerland

[6] Clienia Littenheid AG, Private Clinic for Psychiatry and Psychotherapy, Littenheid, Switzerland

[7] Research Center for Movement Control and Neuroplasticity, Department of Movement Sciences, KU Leuven, Leuven, Belgium

[8] GGZ centraal, Top Referent Trauma Centrum, Ermelo, the Netherlands

[9] Department of Psychosis Studies, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom

[10] Research Unit for Plasticity and Learning of the Healthy Aging Brain, University of Zurich, Switzerland

[11] Department of Psychiatry, VU University Medical Center, Amsterdam, The Netherlands

^ These authors have contributed equally to the manuscript

* These authors have contributed equally to the manuscript

§ Corresponding author

Correspondence to:

A.A.T. Simone Reinders, PhD

Department of Psychological Medicine

Institute of Psychiatry, Psychology and Neuroscience (IoPPN)

King's College London

De Crespigny Park

London SE5 8AZ

United Kingdom

E-mail: a.a.t.s.reinders@gmail.com; a.a.t.s.reinders@kcl.ac.uk

Running Title: Aiding the diagnosis of DID using brain biomarkers

Number of words (max 4000): 3797

Number of References (excluding Methods): 25

Number of Tables + Figures = 3 out of 4 allowed & 1 Supplementary Table

ABSTRACT

Background: A diagnosis of Dissociative identity disorder (DID) is controversial and prone to under- and misdiagnosis. From the moment of seeking treatment for symptoms to the time of an accurate diagnosis of DID individuals received an average of four prior other diagnoses and spent seven years, with reports of up to twelve years, in mental health services.

Aim: To investigate whether data-driven pattern recognition methodologies applied to structural brain images can provide biomarkers to aid DID diagnosis.

Method: Structural brain images of 75 participants were included; 32 female individuals with DID and 43 matched healthy controls. Individuals with DID were recruited from psychiatry and psychotherapy outpatient clinics. Probabilistic pattern classifiers were trained to discriminate cohorts based on measures of brain morphology.

Results: The pattern classifiers were able to accurately discriminate between individuals with DID and healthy controls with high sensitivity (72%) and specificity (74%) on the basis of brain structure. These findings provide evidence for a biological basis for distinguishing between DID affected and healthy individuals.

Conclusions: We propose a pattern of neuroimaging biomarkers that could be used to inform the identification of individuals with DID from healthy controls at the individual level. This is important and clinically relevant because the DID diagnosis is controversial and individuals with DID are often misdiagnosed. Ultimately, the application of pattern recognition methodologies could prevent unnecessary suffering of individuals with DID because of an earlier accurate diagnosis, which will facilitate faster and targeted interventions.

Declaration of interest: The authors declare no competing financial interests.

Access to data: Antje A.T. S. Reinders confirms to have access to all the data in the study.

INTRODUCTION

Dissociative identity disorder (DID)[1] is probably the most disputed psychiatric disorder[2,3]. DID is the most severe of dissociative disorders and involves two or more dissociative personality states, recurrent gaps in the recall of everyday events or important personal information, and/or traumatic events that are inconsistent with ordinary forgetting, and is not related to substance abuse or general medication. For decades the disorder has been officially recognized in the Diagnostic and Statistical Manual of Mental Disorders (DSM) (in the DSM-III (1980) as Multiple Personality Disorder), but many patients with DID share a history of years of misdiagnoses, inefficient pharmacological treatment, and several hospitalizations[4]. To date, many clinicians and scientists still question the validity and even the very existence of DID[5,6]. Unfamiliarity with the spectrum of dissociative disorders and lack of knowledge and appreciation of its epidemiology[7], the existence of imitative DID, as well as the reluctance of individuals with DID to present their dissociative symptoms, often due to feelings of shame, may lead to the validity concerns and under- and misdiagnosis of DID. Years of incorrect treatment results in protracted personal suffering and high direct and indirect societal costs[8,9]. Structural brain imaging holds promise to aid disease diagnosis by providing objective biomarkers at the single subject level[10], thereby paving the way for a fast and correct diagnosis of individuals with DID. The current study presents a first step towards an automated classification of individuals with DID by investigating whether individuals with DID can be separated from healthy controls on the basis of neuroimaging markers, thus informing DID's neuroanatomical basis in terms of grey and white matter of the brain.

Skeptics of DID assume that dissociative symptoms can easily be simulated by normal healthy individuals, which comprises the Fantasy Model of DID[11]. Several pioneering functional brain imaging studies from our group have shown that individuals with genuine DID can be distinguished from healthy controls simulating DID[12–14], but critics could still argue that subjects can manipulate their brain activity[15,16]. As neuroanatomical data is unlikely to be subject to cognitive manipulation, in this study we investigate whether patients with DID can be separated from healthy controls at the individual subject level on the basis of neuroanatomical biomarkers by employing a multivariate data driven pattern recognition approach. We used a probabilistic pattern recognition approach[10] that allowed us to investigate the diagnostic value of grey and white matter of the brain in a comparatively large sample of individuals with DID as compared to healthy controls and to quantify the degree to which the brain phenotype of DID patients can be distinguished from those of healthy subjects. This study is important in two ways: 1) it provides evidence as to whether genuine DID can be distinguished from normal healthy individuals on the basis of their brain morphology, thereby addressing the core of the Fantasy Model for DID, and 2) it provides

neuroanatomical biomarkers that could support the development of pattern recognition methodologies to be used as a clinically useful aid for the diagnostic accuracy of DID.

METHODS

Subjects

Magnetic resonance imaging (MRI) data from 75 participants were obtained in the Netherlands in the University Medical Centre in Groningen (UMCG, the Netherlands) and the Amsterdam Medical Centre (AMC, the Netherlands), and in Switzerland at the University Hospital in Zurich (USZ). Details of these two samples have previously been published elsewhere: Chalavi et al.[17,18] (Dutch sample), Schlumpf et al.[12,13] (Swiss/German sample), and Reinders et al.[19] (combined). All participants gave informed written consent in accordance with the Declaration of Helsinki and as dictated by ethics approval obtained by the Medical Ethical Committees (METc) of the University Medical Center Groningen (UMCG) and the Amsterdam Medical Center (AMC), and by the cantonal ethical commission of Zurich.

Overall, 32 women with DID were recruited from private practitioners of psychiatry and psychotherapy and psychiatric outpatient departments and initially diagnosed according to DSM-IV criteria for DID[20]. The clinical diagnosis was subsequently confirmed by independent expert clinicians using the Structural Clinical Interview for DSM-IV Dissociative Disorders (SCID-D)[21,22], specifically to avoid the inclusion of imitative DID[23]. DID is known to be highly comorbid[24,25]. In the current study PTSD co-morbidity was debriefed using the SCID-D and it was found that out of the 32 DID individuals 29 individuals had co-morbid PTSD and 3 individuals had PTSD in remission. The following information concerning other comorbid disorders was obtained based on DSM-IV classification [American Psychiatric Association, 1994] from the participants and/or their personal therapists (N=29): no other comorbid disorders (N=13), somatoform disorder (N=2), depression (chronic N=1, recurrent N=10), dysthymic disorder (N=1), specific phobias (N=3), panic disorder (N=3), anxiety disorder (N=1), obsessive compulsive disorder (N=1), personality disorders (not otherwise specified (N=2), mixed (N=2), borderline personality disorder (N=5), dependent and histrionic (N=1)), eating disorder (N=3), sleeping disorder (N=2), catalepsy (N=1), psychogenic seizures (N=1), and attention deficit disorder (N=1). Of note, as approximately half of the DID subjects did not have any other co-morbidities than PTSD and other co-comorbidities were more randomly distributed across the sample, it is unlikely that these contribute to the classifier in a systematic manner. Nevertheless, even if there is an influence of co-morbidity on classification then our results are likely to represent an underestimation of classification strength and a more homogeneous sample would increase the sensitivity and specificity.

The DID and healthy control (HC) group were carefully matched for demographics including age, gender (all female), years of education, and Western European ancestry. As previously shown[19], we indeed did not find any significant differences between patients and HCs with respect to age or education (see Supplementary Table 1). As part of the inclusion it

was confirmed that all HCs were free of medication and psychiatric disorders. Furthermore, they scored below a critical cut-off of 25 on the Dissociative Experiences Scale (DES[26]) and 29 on the Somatoform Dissociation Questionnaire (SDQ-20[27]). Depersonalization symptoms were assessed using the Cambridge Depersonalization Scale (CDS[28]). Traumatic experiences were measured with the Traumatic Experience Checklist (TEC[29]). As expected and previously reported[19], psychoform and somatoform dissociative symptoms and depersonalization scores were significantly higher in the DID group as compared to HCs (all p values < 0.001). Individuals with DID also scored significantly higher compared to the controls for traumatic experiences (all p values < 0.001) on all five adverse life event categories, namely emotional neglect, emotional abuse, physical abuse, sexual abuse, and sexual harassment (see Supplementary Table 1).

MRI

Data Acquisition

All data were obtained on 3-T Philips whole-body MRI scanners (Philips Medical Systems, Best, NL) in one of the three participating centers. An optimized structural MRI protocol[30] with high reproducibility between centers was used at all three centers and T1-weighted anatomical MR scans were acquired (3D MPRAGE, TR=9.95ms, TE=5.6ms, flip-angle=8º, 1x1x1mm^3 voxels, number of slices=160, total scan-time=10m14s).

DID patients and healthy controls (HCs) were scanned interleaved (i.e., alternating between patients and healthy controls) within a short time interval. Final samples were distributed relatively equally over the three centers, with 10 patients and 17 HC included from the UMCG, 7 patients and 11 HC from the AMC, and 15 patients and 15 HC from Zurich. The number of participants in each group also did not differ across centers (Chi square=1.01, p=0.603).

Image preprocessing

After quality control checks, structural images were preprocessed using the SPM8 software (http://www.fil.ion.ucl.ac.uk/spm/, release 4667). They were first segmented into different tissue types via the “new segment” tool[31], which is part of the voxel based morphology (VBM) processing pipeline. Rigidly aligned grey and white matter maps, down-sampled to 1.5 mm isotropic voxel size, were then used to diffeomorphically register all subjects to their common average (i.e., study-specific template), using a matching term that assumed a multinomial distribution[32]. Registration involved estimating a set of initial velocities, from which the deformations were computed by a geodesic shooting procedure[33]. Classification was based on a set of “scalar momentum” image features derived from this registration, which describe anatomical variability amongst subjects[34]. These images contain all

information necessary to reconstruct the original images (in addition to the template) and therefore provide a parsimonious representation of shape difference. The scalar momentum images for grey and white matter were spatially smoothed with an isotropic 10mm Gaussian kernel and concatenated prior to classification. This choice of feature construction method and smoothing level was based on previous work, where smoothed scalar momentum images yielded greater accuracy than a range of alternative features (including Jacobian determinants, rigidly aligned grey matter, spatially normalised grey matter and Jacobian scaled spatially normalised grey matter) for predicting subject age and sex in a publicly available dataset[35] and for discriminating neurological disorders from structural MRI[35].

Pattern Recognition

Binary Gaussian process classifiers (GPCs[36]) were used as the primary analytical approach for this study. GPCs are a supervised pattern recognition approach that assigns a predictive probability of group membership to each individual based on a set of "training" data. They are kernel classifiers similar to the widely used Support Vector Machines (SVMs) and have shown high levels of performance for neuroimaging data[37–39]. Moreover, GPCs have advantages over SVMs in that the probabilistic predictions they provide encode a measure of predictive confidence that quantifies diagnostic uncertainty and can capture variability within clinical groups. More importantly, probabilistic predictions can be easily adjusted to compensate for the prior frequency of diagnostic classes in experimental populations. This means that inference remains coherent in classification scenarios where the frequency of each class in the test set is different from the frequencies observed in the training set and is useful to accommodate variations in disease prevalence[40] and to compensate for unbalanced training datasets[41] as outlined below. These properties are particularly important for the present study because the classes are unbalanced and the number of samples available for training is small.

Linear binary GPCs were used to discriminate DID patients from healthy controls. Technical details surrounding GPC inference have been presented elsewhere[37]. A leave-one-subject-out cross-validation approach was used to assess classifier generalizability, whereby a single subject was excluded to comprise the test set, and all parameters were inferred from the remaining data (training set), before applying this classifier to predict the labels for the test samples. Prior to classification, a t-test was used to select a set of discriminant voxels using a fixed threshold of $p < 0.001$. This was repeated excluding each subject once. Importantly, feature selection was performed using the training data only, which ensures the classifier remains unbiased.

Classifier performance was evaluated using receiver operating characteristic (ROC) curves derived from the probabilistic predictions and classification accuracy, which measures

the classifier performance in a categorical sense. To derive categorical predictions from the probabilistic predictions obtained from the GPC, the probabilistic predictions were thresholded according to the frequency of classes in the training set (i.e. 0.5 if the classes are balanced). Classifier assessment metrics included the sensitivity and specificity in addition to the positive and negative predictive value (PPV/NPV). Finally the (balanced) accuracy was computed as the mean of sensitivity and specificity, which quantifies the overall categorical classification performance of the classifier in a way that accommodates potential class imbalance in the data.

Forward maps of regional class differences

To understand the relative importance of different brain regions underlying the classification decision, we employed a forward mapping strategy[42]. This has advantages over the more commonly used strategy of directly mapping the weight vector[43]. Specifically, a voxel may have a high weight because of an association with the class labels or as a result of high collinearity between voxels, where the high weight may help to cancel out noise or mismatch in other voxels. In contrast, the coefficients from the forward modeling approach proposed by Haufe and colleagues[42] represent the group differences between classes, which are more often of interest when interpreting a trained classifier. In this case stronger positive values in a forward map indicate a stronger association of a region with the DID (“Favouring DID”), that is, increased volume of a brain area in DID, while negative values indicate a stronger association with HCs (“Favouring HC”), that is, decreased volume of a brain area in DID. Note that only voxels surviving the univariate feature selection step are included in the map and that the GPC discriminates data on the basis of the whole pattern. Hence, local inferences based on these approaches should be made with caution. In order to report results in standard MNI coordinates the DARTEL group tissue template (GM, WM and CSF) was coregistered to a SPM8 new_segment segmentation of the FSL MNI152_T1_1mm template brain. Advanced normalisation tools (ANTS version 2.1.0[44]) were used to calculate a non-linear transformation employing the SyN algorithm (antsRegistrationSyN.sh, default parameters) using multimodal information from the 3 channels (CSF, GM and WM). The results of the registration were visually inspected and appeared to be a significant improvement on a simple affine registration. We selected the cluster peaks of the forward maps in terms of X, Y, and Z coordinates on the basis of the maximum (absolute) coefficient. Anatomical labels were derived by AATSR, SC and YRS from a consensus of different atlases.

RESULTS

Classification

Using the imaging data, the classifier discriminated between DID and HC groups with high sensitivity (71.88%) and specificity (73.81%), yielding an overall balanced accuracy of 72.84%, which was significantly higher than the accuracy expected by chance ($p < 0.01$, permutation test). Receiver operating characteristic analysis (see Figure 1) further demonstrated that classification performance was above chance across all decision thresholds and yielded an area under the curve of 0.74. The forward maps for the grey and white matter components are displayed in Figure 2. Brain areas contributing to the classification are listed in Table 1.

Relative decrease in regional volume in the DID group

For grey matter, the pattern of voxels favouring HC, that is a relative increase for the HC group or in other words a relative decrease in the DID group, included bilateral middle, superior, and dorsolateral frontal gyrus, left medial and right orbito-frontal gyrus, bilateral anterior cingulate gyrus, bilateral middle temporal gyrus, bilateral fusiform gyrus, right inferior temporal gyrus, left inferior parietal lobule and supramarginal gyrus, and bilateral superior occipital gyrus.

For white matter, the pattern of voxels favouring HC included the bilateral inferior fronto-occipital tract, the left corticospinal tract, and the right superior and left inferior longitudinal fasciculus. In addition, the white matter of the right inferior, bilateral middle and superior frontal regions, bilateral temporal, cerebellar, and lateral occipital regions, and of the left amygdala-hippocampal junction, and (anterior) cingulate were also included in the distinguishing pattern.

Relative increase in regional volume for the DID group

For grey matter the pattern of voxels favouring DID was found to be far less pronounced than that of favouring HC, and included left superior frontal gyrus, left medial parietal lobule, and bilateral cerebellum.

The pattern of voxels in the white matter of the brain favouring DID included left inferior and superior longitudinal fasciculus, the left inferior fronto-occipital fasciculus, and the right corticospinal tract. In addition, the white matter of bilateral (anterior) cingulate and insula regions, bilateral inferior, medial and superior frontal regions, left parietal regions and putamen, right inferior and middle temporal regions and bilateral cerebellum were included.

DISCUSSION

Main findings

This is the first study to demonstrate that individuals with DID and healthy controls can be differentiated at the level of individual subjects with a high level of accuracy on the basis of their neuroanatomical markers. This discrimination was based on neuroanatomical data in the largest sample of individuals with DID included in a brain imaging study to date. We found widespread grey and white matter spatially dependent patterns of abnormal brain morphology in individuals with DID as compared to healthy controls. These findings are important because they provide evidence for a biological basis for distinguishing between genuine DID and healthy controls. The current study also provides support for the development of pattern recognition methodologies as a clinically useful diagnostic tool in DID thereby paving the way for future studies with a diagnostic aim in distinguishing between genuine DID and other psychopathologies.

Comparison to other studies

Despite the reported high prevalence of DID of approximately 6% in psychiatric outpatients[45] and 1-3% of the general population[46], neurobiological studies on DID are scarce[17,19,47] and depend on mass-univariate data-analysis approaches, which provide inferences at the group level. Mass-univariate data-analysis ignore information encoded by spatially distributed patterns of morphological abnormalities throughout the brain and have limited ability to provide inferences at the level of individual participants. In contrast, multivariate data-analysis techniques using pattern classification methodology allow for the study of underlying patterns of effects and the distribution across brain regions, and more importantly, they provide predictions that quantify group separation at the level of individual subjects on the basis of patterns of abnormality in the data, which may be clinically useful[10].

Pattern recognition methods are becoming widely used for neuroimaging-based psychiatric diagnostics[10]. Our study shows that DID patients can be distinguished from healthy controls at an individual level with a sensitivity of 71.88% and specificity of 73.81%. This level of accuracy is comparable to what has been demonstrated for most psychiatric disorders[10], including psychosis[48]. Our results provide evidence that DID has a biological basis that allows individuals with DID to be separated from controls at the level of individual subjects. This is important because of the controversy surrounding DID as a diagnostic entity[2]. Skeptics of DID assume that dissociative symptoms can easily be simulated by normal healthy individuals and they argue that subjects can manipulate their brain activity[15,16]. As neuroanatomical data is unlikely to be subject to cognitive manipulation the current study challenges the core of the Fantasy Model for DID by providing evidence that genuine DID can be distinguished from normal healthy individuals on the basis of their brain

morphology. Currently the DID diagnosis is made based solely on clinical interview and observation. Unfamiliarity with the spectrum of dissociative disorders, validity concerns of DID, the existence of imitative DID, or lack of knowledge and appreciation of the epidemiology could lead to under- and misdiagnosis by clinicians[4]. High comorbidity rates complicate the diagnosis even further. Applying pattern recognition methods to brain imaging data of DID patients offers a biomarker approach that can complement, aid and improve clinical decision making. This could reduce misdiagnoses, treatment time, treatment costs, and ultimately improve patient's quality of life.

Neuroanatomical biomarkers

According to the Trauma Model[11] DID is an early-onset form of post-traumatic stress disorder (PTSD)[11,17,18] . Early life stressors may have long-lasting detrimental effects on neurobiology due to altered stress reactivity following childhood trauma[19]. Earlier neuroanatomical studies in DID have focused on, and found, smaller hippocampal volume, which seems to be the results of exposure to stress hormones due to antecedent traumatization. Although it is currently unknown how early traumatization affects the development of the brain[19] it is not surprising that long-lasting trauma results in a widespread patterns of affected grey and white matter brain regions. We found affected brain regions in different lobules in the brain, but most prominently in the frontal grey and white matter regions, supporting findings from previous studies investigating the neuroanatomical correlates of dissociative symptoms across disorders[17,49–51] using univariate data-analysis approaches. Interestingly, the pattern of affected grey matter structural regions in the current study shows overlap with regions found in functional brain imaging studies involving dissociation, which included different patient samples and different paradigms, such as resting state in dissociative PTSD[52], script-driven imagery in DID[14] or emotion processing in depersonalization disorder[53], but consistently reported functional aberrations in frontal regions of the brain. Models of trauma-related dissociation[14,52] propose important roles for the cingulate gyrus, medial prefrontal cortex, and superior frontal regions in emotion under-/overregulation and dissociation. The current multivariate study in the most severe form of dissociative disorders found that structural aberrations of these brain regions are part of the identified spatially distributed pattern. We therefore propose that future research into dissociation and DID focuses on these specific prefrontal areas, as well as the middle and dorsolateral prefrontal cortex, as important candidate regions for identifying neurobiomarkers of dissociation and specifically of DID.

Limitations

Our study has several strengths and limitations. First, while the findings show that DID patient can be distinguished from healthy controls at an individual level with a high sensitivity and specificity, future studies are needed to unravel how individuals with DID differ from their most common misdiagnosed psychopathologies, such as borderline personality disorder and schizophrenia. We recommend that such future studies carefully debrief past psychiatric and neurological history including depressive and/or psychotic episodes, history of epilepsy, and duration of treatment, because these factors are likely to improve the ability for differential diagnostics of the classifier. The validation of the complex pattern recognition system with respect to these factors is important for clinical utilization and will need large patient samples of a wide variety of psychopathology. Furthermore, we recommend that future studies include a PTSD group without dissociative symptoms to investigate how PTSD co-morbidity affects the classification, both at the level of the clinical presentation and biology. However, it is important to note that there is negligible overlap between results from the only multivariate study in PTSD[54] and our results, indicating that the multivariate patterns found in the current study are likely to be dissociation-specific neuroanatomical biomarkers. Second, we employed a multicentre acquisition protocol to overcome single-site recruitment limitations, but carefully matched MRI acquisition parameters across sites using a study optimized scanning sequence[30]. We further accounted for inter-site effects during the data-analyses by standardizing the data within each site separately prior to classification, which speaks against the possibility that inter-site effects can be fully attributed to site effects. Third, only women volunteered to participate in the study and therefore the results cannot be extended to all DID patients. Most of these women were currently using medication or had used medication in the past (see Supplementary Table 1). However, because medication use was highly variable across subjects it is unlikely that the effects on grey and white matter will be consistent, as previously reported in a separate study of our group[17]. Nevertheless, even though this is the case in the current study it is recommended that future studies systematically investigate whether neuroanatomical changes are related to psychotropic medication.

Conclusions

In sum, our results reveal patterns of neuroanatomical alterations which overlap with previous findings from functional brain imaging studies. We propose a pattern of neuroimaging biomarkers that could be used to inform the identification of individuals with DID from healthy controls at the individual level. Furthermore, the current study supports the development of pattern recognition methodologies as a clinically useful diagnostic tool and paves the way for future studies that distinguish between DID and other psychopathologies.

This is important and clinically relevant because the DID diagnosis is controversial and individuals with DID are often misdiagnosed. Ultimately, the application of pattern recognition methodologies could prevent unnecessary suffering of individuals with DID because of an earlier accurate diagnosis, which will facilitate faster and targeted interventions.

ACKNOWLEDGEMENTS

This paper represents independent research part funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. A.A.T.S. Reinders was supported by the Netherlands Organization for Scientific Research (www.nwo.nl), NWO-VENI grant no. 451-07-009. S. Chalavi is supported by a David Caul graduate research grant from the International Society for the Study of Trauma and Dissociation (ISSTD) (http://www.isst-d.org/about/awards.htm). Andre F. Marquand gratefully acknowledges support from the King's College London Centre of Excellence in Medical Engineering, funded by the Wellcome Trust and EPSRC and from a VIDI fellowship from the NWO (grant no. 016.156.415). Yolanda Schlumpf was supported by the Forschungskredit of the University of Zurich. The authors would like to thank all the participants and their therapists. We also would like to thank Nel Draijer, Mechteld Giesen, Ekaterina Weder, and Eva Zimmermann for participant inclusion and scanning and Andrew Lawrence for coordinate transformation into MNI space and preparing the Tables.

AUTHOR CONTRIBUTIONS

1) Conception and design: A.A.T.S.R., Y.R.S., E.M.V., E.R.S.N., P.D., L.J., D.J.V.
2) Analysis and interpretation of data: A.A.T.S.R., A.F.M., S.C., D.J.V.
3) Drafting the article: A.A.T.S.R., A.F.M., D.J.V.
4) Critical revision for important intellectual content: S.C., Y.R.S., E.M.V., E.R.S.N., P.D., L.J.
3) Final approval of the version to be published: A.A.T.S.R., A.F.M., S.C., Y.R.S., E.M.V., E.R.S.N., P.D., L.J., D.J.V.

REFERENCES

1 Gillig PM. Dissociative identity disorder: a controversial diagnosis. *Psychiatry* 2009; **6**: 24–9.

2 Dalenberg CJ, Brand BL, Loewenstein RJ, Gleaves DH, Dorahy MJ, Cardeña E, *et al.* Reality versus fantasy: reply to Lynn et al. (2014). *Psychol Bull* 2014; **140**: 911–20.

3 Brand BL, Vissia EM, Chalavi S, Nijenhuis ERS, Webermann AR, Draijer N, *et al.* DID is trauma based: further evidence supporting the trauma model of DID. *Acta Psychiatr Scand* 2016; **134**: 560–3.

4 Chu JA, Dell PF, Van der Hart O, Cardeña E, Barach PM, Somer E, *et al.* Guidelines for Treating Dissociative Identity Disorder in Adults, Third Revision - International Society for the Study of Trauma and Dissociation. *J Trauma Dissociation* 2011; **12**: 115–87.

5 Piper A, Merskey H. The persistence of folly: a critical examination of dissociative identity disorder. Part I. The excesses of an improbable concept. *Can J Psychiatry* 2004; **49**: 592–600.

6 Pope HG, Barry S, Bodkin A, Hudson JI. Tracking scientific interest in the dissociative disorders: a study of scientific publication output 1984-2003. *Psychother Psychosom* 2006; **75**: 19–24.

7 Sar V. Epidemiology of Dissociative Disorders: An Overview. *Epidemiol Res Int* 2011; **1**: 1–8.

8 Lloyd M. Reducing the cost of dissociative identity disorder: Measuring the effectiveness of specialized treatment by frequency of contacts with mental health services. *J Trauma Dissociation* 2016; **17**: 362–70.

9 Myrick AC, Webermann AR, Langeland W, Putnam FW, Brand BL. Treatment of dissociative disorders and reported changes in inpatient and outpatient cost estimates. *Eur J Psychotraumatol* 2017; **8**: 1375829.

10 Wolfers T, Buitelaar JK, Beckmann C, Franke B, Marquand AF. From estimating activation locality to predicting disorder: a review of pattern recognition for neuroimaging-based psychiatric diagnostics. *Neurosci Biobehav Rev* 2015; **57**: 328–49.

11 Vissia EM, Giesen ME, Chalavi S, Nijenhuis ERS, Draijer N, Brand BL, *et al.* Is it Trauma- or Fantasy-based? Comparing dissociative identity disorder, post-traumatic stress disorder, simulators, and controls. *Acta Psychiatr Scand* 2016; **134**: 111–28.

12 Schlumpf YR, Nijenhuis ERS, Chalavi S, Weder E V, Zimmermann E, Luechinger R, *et al.* Dissociative part-dependent biopsychosocial reactions to backward masked angry and neutral faces: An fMRI study of dissociative identity disorder. *NeuroImage Clin* 2013; **3**: 54–64.

13 Schlumpf YR, Reinders AATS, Nijenhuis ERS, Luechinger R, van Osch MJP, Jäncke L. Dissociative part-dependent resting-state activity in dissociative identity disorder: a controlled FMRI perfusion study. *PLoS One* 2014; **9**: e98795.

14 Reinders AATS, Willemsen ATM, Vissia EM, Vos HPJ, den Boer JA, Nijenhuis ERS. The Psychobiology of Authentic and Simulated Dissociative Personality States: The Full Monty. *J Nerv Ment Dis* 2016; **204**: 445–57.

15 Zotev V, Phillips R, Young KD, Drevets WC, Bodurka J. Prefrontal control of the amygdala during real-time fMRI neurofeedback training of emotion regulation. *PLoS One* 2013; **8**: e79184.

16 Kim S, Birbaumer N. Real-time functional MRI neurofeedback: a tool for psychiatry. *Curr Opin Psychiatry* 2014; **27**: 332–6.

17 Chalavi S, Vissia EM, Giesen ME, Nijenhuis ERS, Draijer N, Barker GJ, *et al.* Similar cortical but not subcortical gray matter abnormalities in women with posttraumatic stress disorder with versus without dissociative identity disorder. *Psychiatry Res* 2015; **231**: 308–19.

18 Chalavi S, Vissia EM, Giesen ME, Nijenhuis ERS, Draijer N, Cole JH, *et al.* Abnormal hippocampal morphology in dissociative identity disorder and post-traumatic stress disorder correlates with childhood trauma and dissociative symptoms. *Hum Brain Mapp* 2015; **36**: 1692–704.

19 Reinders AATS, Chalavi S, Schlumpf YR, Vissia EM, Nijenhuis ERS, Jäncke L, *et al.* Neurodevelopmental origins of abnormal cortical morphology in dissociative identity disorder. *Acta Psychiatr Scand* 2017. doi:10.1111/acps.12839.

20 APA. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, DSM-5. Am. Psychiatr. Assoc. 2013; : Fifth Edition. Arlington, VA.

21 Boon S, Draijer N. Multiple personality disorder in The Netherlands: a clinical investigation of 71 patients. *Am J Psychiatry* 1993; **150**: 489–94.

22 Steinberg M. *Structured Clinical Interview for DSM-IV Dissociative Disorders (SCID-D).* American Psychiatric Press, 1993.

23 Draijer N, Boon S. The Imitation of Dissociative Identity Disorder: Patients at Risk, Therapists at Risk. *J Psychiatry Law* 1999; **27**: 423–58.

24 Rodewald F, Wilhelm-G?ling C, Emrich HM, Reddemann L, Gast U. Axis-I Comorbidity in Female Patients With Dissociative Identity Disorder and Dissociative Identity Disorder Not Otherwise Specified. *J Nerv Ment Dis* 2011; **199**: 122–31.

25 Bozkurt H, Duzman Mutluer T, Kose C, Zoroglu S. High psychiatric comorbidity in adolescents with dissociative disorders. *Psychiatry Clin Neurosci* 2015; **69**: 369–74.

26 Bernstein EM, Putnam FW. Development, reliability, and validity of a dissociation scale. *J Nerv Ment Dis* 1986; **174**: 727–35.

27 Nijenhuis ERS, Spinhoven P, Van Dyck R, Van der Hart O, Vanderlinden J. The development and psychometric characteristics of the Somatoform Dissociation Questionnaire (SDQ-20). *J Nerv Ment Dis* 1996; **184**: 688–94.

28 Sierra M, Berrios GE. The Cambridge Depersonalization Scale: a new instrument for the measurement of depersonalization. *Psychiatry Res* 2000; **93**: 153–64.

29 Nijenhuis ERS, Van der Hart O, Kruger K. The psychometric characteristics of the Traumatic Experiences Checklist (TEC): first findings among psychiatric outpatients. *Clin Psychol Psychother* 2002; **9**: 200–10.

30 Chalavi S, Simmons A, Dijkstra H, Barker GJ, Reinders AA. Quantitative and qualitative assessment of structural magnetic resonance imaging data in a two-center study. *BMC Med Imaging* 2012; **12**: 27.

31 Ashburner J, Friston KJ. Unified segmentation. *Neuroimage* 2005; **26**: 839–51.

32 Ashburner J, Friston KJ. Computing average shaped tissue probability templates. *Neuroimage* 2009; **45**: 333–41.

33 Ashburner J, Friston KJ. Diffeomorphic registration using geodesic shooting and Gauss-Newton optimisation. *Neuroimage* 2011; **55**: 954–67.

34 Singh N, Fletcher PT, Preston JS, Ha L, King R, Marron JS, *et al.* Multivariate Statistical Analysis of Deformation Momenta Relating Anatomical Shape to Neuropsychological Measures. In *13th International Conference on Medical Image Computing and Computer-Assisted Intervention, MICCAI 2010*: 529–37. , 2010.

35 Marquand AF, Filippone M, Ashburner J, Girolami M, Mourao-Miranda J, Barker GJ, *et al.* Automated, High Accuracy Classification of Parkinsonian Disorders: A Pattern Recognition Approach. *PLoS One* 2013; **8**. doi:10.1371/journal.pone.0069237.

36 Rasmussen CE, Rasmussen CE. Gaussian processes for machine learning. 2006. (http://citeseerx.ist.psu.edu/viewdoc/summary?doi=10.1.1.86.3414).

37 Marquand A, Howard M, Brammer M, Chu C, Coen S, Mourão-Miranda J. Quantitative prediction of subjective pain intensity from whole-brain fMRI data using Gaussian processes. *Neuroimage* 2010; **49**: 2178–89.

38 Orrù G, Pettersson-Yeo W, Marquand AF, Sartori G, Mechelli A. Using Support Vector Machine to identify imaging biomarkers of neurological and psychiatric disease: a critical review. *Neurosci Biobehav Rev* 2012; **36**: 1140–52.

39 Schrouff J, Rosa MJ, Rondina JM, Marquand AF, Chu C, Ashburner J, *et al.* PRoNTo: Pattern Recognition for Neuroimaging Toolbox. *Neuroinformatics* 2013; **11**: 319.

40 Hahn T, Marquand AF, Plichta MM, Ehlis A-C, Schecklmann MW, Dresler T, *et al.* A Novel Approach to Probabilistic Biomarker-Based Classification Using Functional Near-Infrared Spectroscopy. *Hum Brain Mapp* 2013; **34**: 1102.

41 Lim HK, Jung WS, Ahn KJ, Won WY, Hahn C, Lee SY, *et al.* Regional cortical

thickness and subcortical volume changes are associated with cognitive impairments in the drug-naive patients with late-onset depression. *Neuropsychopharmacology* 2012; **37**: 838–49.

42 Haufe S, Meinecke F, Gorgen K, Dahne S, Haynes J-D, Blankertz B, *et al.* On the interpretation of weight vectors of linear models in multivariate neuroimaging. *Neuroimage* 2014; **87**: 96–110.

43 Mourão-Miranda J, Bokde ALW, Born C, Hampel H, Stetter M. Classifying brain states and determining the discriminating activation patterns: Support Vector Machine on functional MRI data. *Neuroimage* 2005; **28**: 980–95.

44 Avants BB, Tustison NJ, Song G, Cook PA, Klein A, Gee JC. A reproducible evaluation of ANTs similarity metric performance in brain image registration. *Neuroimage* 2011; **54**: 2033–44.

45 Foote B, Smolin Y, Kaplan M, Legatt ME, Lipschitz D. Prevalence of dissociative disorders in psychiatric outpatients. *Am J Psychiatry* 2006; **163**: 623–9.

46 Sar V, Akyüz G, Doğan O. Prevalence of dissociative disorders among women in the general population. *Psychiatry Res* 2007; **149**: 169–76.

47 Dorahy MJ, Brand BL, Sar V, Krüger C, Stavropoulos P, Martínez-Taboas A, *et al.* Dissociative identity disorder: An empirical overview. *Aust N Z J Psychiatry* 2014; **48**: 402–17.

48 Mourao-Miranda J, Reinders AATS, Rocha-Rego V, Lappin J, Rondina J, Morgan C, *et al.* Individualized prediction of illness course at the first psychotic episode: a support vector machine MRI study. *Psychol Med* 2012; **42**: 1037–47.

49 Nardo D, Högberg G, Lanius RA, Jacobsson H, Jonsson C, Hällström T, *et al.* Gray matter volume alterations related to trait dissociation in PTSD and traumatized controls. *Acta Psychiatr Scand* 2013; **128**: 222–33.

50 Sierra M, Nestler S, Jay E-L, Ecker C, Feng Y, David AS. A structural MRI study of cortical thickness in depersonalisation disorder. *Psychiatry Res Neuroimaging* 2014; **224**: 1–7.

51 Daniels JK, Frewen P, Theberge J, Lanius RA. Structural brain aberrations associated with the dissociative subtype of post-traumatic stress disorder. *Acta Psychiatr Scand* 2016; **133**: 232–40.

52 Lanius RA, Vermetten E, Loewenstein RJ, Brand B, Schmahl C, Bremner JD, *et al.* Emotion modulation in PTSD: Clinical and neurobiological evidence for a dissociative subtype. *Am J Psychiatry* 2010; **167**: 640–7.

53 Lemche E, Anilkumar A, Giampietro VP, Brammer MJ, Surguladze SA, Lawrence NS, *et al.* Cerebral and autonomic responses to emotional facial expressions in depersonalisation disorder. *Br J Psychiatry* 2008; **193**: 222–8.

54 Gong Q, Li L, Tognin S, Wu Q, Pettersson-Yeo W, Lui S, *et al.* Using structural neuroanatomy to identify trauma survivors with and without post-traumatic stress disorder at the individual level. *Psychol Med* 2014; **44**: 195–203.

TABLE LEGEND

Table 1

Grey and white matter patterns of affected brain regions. *DID* < *HC*: negative values in a forward map indicate a stronger association with HCs (“Favouring HC”), that is, a relative decreased volume of a brain area in DID. *DID* > *HC*: positive values in a forward map indicate a stronger association of a region with the DID (“Favouring DID”), that is, relative increased volume of a brain area in DID. Only clusters larger than an arbitrary threshold of eight voxels[14] are shown.

TABLE 1

		L/R	BA	X	Y	Z	Volume	MAX
DID < HC *								
GREY MATTER								
Frontal								
	I. Frontal gyrus	L	47	-27.3	25.0	-16.7	1889	20300
	M. Frontal gyrus	L	10	-25.0	63.5	10.5	50	14900
	M. Frontal gyrus	R	10	37.4	58.2	16.4	324	16800
	M. Frontal gyrus	R	8	45.0	14.7	52.7	366	19000
	M. Frontal gyrus/Orbito-Frontal gyrus	R	11	23.0	16.5	-14.5	319	18400
	Medial Frontal gyrus	L	10	-4.5	64.0	-13.5	112	15200
	Medial Frontal gyrus	L	9	-4.5	56.0	40.5	98	17800
	S./Medial Frontal gyrus	L	10	-6.0	65.5	22.5	31	15900
	S. Frontal gyrus	L	6	-6.7	1.5	73.3	40	14900
	S. Frontal sulcus	L	6	-23.0	17.3	66.3	18	13400
	S. Frontal sulcus	R	6	26.5	5.5	70.0	188	16000
	S. Frontal gyrus	R	9	8.0	53.0	45.0	172	19700
	S. Frontal gyrus	R	8	7.5	42.0	56.0	25	11900
	Dorsolateral prefrontal cortex/M. Frontal Gyrus	L	9/46	-51.0	23.5	33.5	814	18600
	Dorsolateral prefrontal cortex/M. Frontal Gyrus	L	9/46	-40.5	41.0	2.5	75	15700
	Dorsolateral prefrontal cortex/M. Frontal Gyrus	R	9/46	44.5	30.3	15.7	324	16300
	Cingulate gyrus	L	24	-9.0	3.0	35.0	70	17100
	Anterior Cingulate Gyrus	L	24	-6.5	37.5	5.5	105	16400
	Anterior Cingulate Gyrus	R	24/32	20.0	36.3	21.3	444	17100
	Precentral gyrus	L	4	-55.0	-9.5	51.5	126	16700
Parietal								
	I. Parietal lobule	L	40	-50.5	-54.0	54.0	25	15000
	I. Parietal lobule	L	40	-59.0	-33.5	50.5	18	13900
	Supramarginal gyrus	L	40	-63.0	-47.3	33.3	16	17000
Occipital								
	I. Occipital gyrus	L	18	-38.3	-89.7	-15.7	50	15400
	M. Occipital gyrus	L	19	-55.5	-71.0	-9.5	306	18500

	S. Occipital sulcus	L	19	-36.0	-87.0	32.5	47	16300
	S. Occipital gyrus	R	19	42.0	-83.0	32.0	30	15700
Temporal								
	I. Temporal gyrus	R	20	45.3	1.5	-43.8	99	18700
	I. Temporal gyrus/Fusiform gyrus	R	37	49.5	-72.0	-4.5	135	14200
	I. Temporal gyrus/Fusiform gyrus	R	20	49.8	-18.4	-23.4	10	14400
	M. Temporal gyrus	R	21	61.3	-35.0	-5.3	259	17500
	M./S. Temporal gyrus	L	21/38	-52.6	5.2	-13.4	26	13200
	M./S. Temporal gyrus	R	21/38	38.0	13.5	-41.5	140	16000
	Fusiform gyrus	L	37	-40.0	-46.5	-6.5	171	15100
Other								
							None	
WHITE MATTER								
Tracts								
	I. Longitudional fasciculus	L		-38.7	-45.7	-15.3	70	0.0669
	S. Longitudinal fasciculus (temporal part)	R		62.6	-37.4	-12.4	181	0.1720
	Corticospinal tract	L		-21.0	-17.5	9.5	24	0.0807
	I. Frontal-Occipital fasciculus	L		-26.0	24.5	16.5	101	0.1190
	I. Frontal-Occipital fasciculus	L		-27.0	37.0	3.0	38	0.0686
	I. Frontal-Occipital fasciculus	R		23.0	34.5	25.5	214	0.1120
Frontal								
	I. Frontal WM	R		23.0	14.5	-19.5	179	0.1150
	M. Frontal WM	R		58.0	32.3	18.3	73	0.0481
	M. Frontal WM	L		-53.0	17.0	41.5	488	0.1880
	M. Frontal WM	R		49.5	12.0	52.5	183	0.1060
	M./S. Frontal WM	R		44.7	48.7	25.5	61	0.0900
	S. Frontal WM	L		-11.5	70.5	0.0	76	0.1170
	S. Frontal WM	L		-4.5	47.0	52.5	56	0.1350
	S. Frontal WM	L		-24.0	33.0	56.0	37	0.1160
	S. Frontal WM	L		-6.0	68.3	22.3	31	0.1060
	S. Frontal WM	L		-23.0	17.3	66.3	18	0.0938
	S. Frontal WM	L		-25.5	65.5	7.5	12	0.0207
	S. Frontal WM	R		24.3	1.0	72.3	111	0.2170

	S. Frontal WM	R		9.0	50.0	50.0	103	0.1920
	S. Frontal WM	R		23.4	68.8	10.4	27	0.0898
	S. Frontal WM	R		9.3	38.0	59.7	25	0.2630
	S. Frontal/Premotor WM	R		8.0	17.0	70.0	54	0.1580
	S. Frontal/Premotor WM	L		-6.5	1.5	76.0	40	0.1990
	Anterior Cingulate WM	L		-5.6	34.2	4.4	73	0.0713
	Cingulate WM	L		-7.5	-0.5	33.5	12	0.0112
	Precentral WM	L		-47.6	1.6	52.6	85	0.0771
	Insular WM	R		29.0	21.5	13.5	36	0.0686
Parietal								
	I. Parietal lobule	L		-57.0	-33.5	53.5	13	0.0844
Occipital								
	Lateral Occipital WM	L		-53.0	-70.0	-10.5	268	0.1300
	Lateral Occipital WM (inferior division)	L		-40.5	-89.5	-11.5	50	0.1430
	Lateral Occipital WM (superior division)	L		-36.5	-83.0	34.5	47	0.1130
	Lateral Occipital WM (superior division)	R		40.3	-75.3	46.0	30	0.1050
	Lateral Occipital WM	R		52.0	-74.0	-11.0	124	0.1760
Temporal								
	I. Temporal gyrus (anterior division)	R		47.0	-8.5	-45.0	40	0.0444
	Temporal pole	L		-42.0	17.5	-34.0	98	0.0890
	Temporal pole	L		-54.0	13.0	-19.0	21	0.1090
	Temporal pole	R		31.5	13.3	-41.7	140	0.2670
Other								
	Amygdala/Hippocampus	L		-26.5	-7.0	-20.5	1286	0.2750
	Cerebellum (Crus I)	L		-32.8	-71.6	-33.0	61	0.0792
	Cerebellum (Crus I)	R		37.5	-63.5	-34.0	85	0.0857
DID > HC **								
GREY MATTER								
Frontal								
	S. Frontal sulcus	L	4/6	-19.5	-13.0	58.5	19	10600
Parietal								
	Medial posterior parietal	L	7	-14.7	-58.0	57.7	16	14700

	Medial posterior parietal/Precuneus	L	7	-14.5	-71.0	57.0	14	15200
Occipital								
							None	
Temporal								
							None	
Other								
	Cerebellum (Crus I)	L		-37.5	-72.0	-33.0	686	15500
	Cerebellum (Crus I)	R		42.5	-63.5	-37.0	285	16900
	Periaqueductal grey	L		-2.5	-30.5	-11.0	58	15000
WHITE MATTER								
Tracts								
	I. Longitudinal fasciculus	L		-41.5	-47.0	-4.5	98	0.1060
	I. Longitudinal fasciculus	L		-42.5	-5.0	-20.5	14	0.0369
	S. Longitudinal fasciculus	L		-50.5	-52.5	54.0	22	0.0608
	S. Longitudinal fasciculus	L		-19.5	-14.4	61.0	19	0.3820
	Corticospinal tract	R		16.3	-2.7	9.5	438	0.2030
	Inferior Fronto-Occipital fasciculus	L		-39.9	40.6	0.6	37	0.1390
Frontal								
	I. Frontal WM	L		-32.5	23.7	-19.7	58	0.0835
	I. Frontal WM	L		-21.7	12.0	-18.3	37	0.0399
	I. Frontal WM (pars triangularis)	R		56.7	28.7	13.5	250	0.1070
	M. Frontal WM	R		44.0	17.7	51.7	174	0.1520
	Medial Frontal WM	L		-4.6	54.6	40.6	42	0.0950
	Medial Frontal/Forceps minor	L		-7.8	62.6	-11.6	35	0.0564
	Medial Frontal/Forceps minor	R		6.5	54.7	37.7	65	0.1820
	S. Frontal WM	L		-33.7	29.0	48.7	274	0.1390
	S. Frontal WM	L		-25.5	64.0	14.5	37	0.0903
	S. Frontal WM	R		36.0	55.7	19.7	233	0.1720
	S. Frontal/Premotor WM	R		22.3	9.5	65.5	18	0.0396
	Precentral/Premotor WM	L		-46.5	2.5	46.5	27	0.1040
	Precentral /Premotor WM	L		-56.4	-7.8	49.4	14	0.0527
	Cingulate WM	L		-11.0	8.0	36.5	57	0.1240
	Anterior Cingulate WM	L		-7.8	38.4	0.6	31	0.0572

	Cingulate WM/Forceps minor	R	15.4	31.4	25.8	207	0.1120
	Insula WM	L	-31.5	23.5	11.0	172	0.1480
	Insula WM	R	33.5	29.5	9.0	97	0.1210
Parietal							
	Superior Parietal lobule	L	-15.0	-55.5	53.5	16	0.2130
	Supramarginal WM (posterior division)	L	-63.0	-47.3	33.3	16	0.0923
	Precuneus WM	L	-14.0	-69.5	53.5	14	0.1860
Occipital							
	M. Occipital WM	R	45.4	-70.4	-4.3	9	0.0510
Temporal							
	Temporal pole	L	-33.4	14.4	-38.6	98	0.0626
	I. Temporal WM (anterior division)	R	46.6	1.4	-45.4	56	0.0755
	M. Temporal WM	R	49.0	-34.0	-8.0	77	0.1490
	Fusiform WM	L	-49.2	-66.6	-17.4	36	0.0401
Other							
	Cerebellum (Crus I)	L	-45.5	-55.0	-28.0	624	0.3260
	Cerebellum (Crus I)	R	44.5	-65.3	-41.3	195	0.1170
	Putamen	L	-31.0	-12.0	1.0	312	0.2000
	Brainstem (Midbrain)	L	-7.0	-29.0	-9.5	58	0.1650

* = Favouring HC; negative values in the forward map
** = Favouring DID; positive values in the forward map
M. = Middle

I. = Inferior

S. = Superior

(x, y, z) = coordinates in MNI space

Volume in voxels

MAX = weight vector score

FIGURES & FIGURE LEGENDS

Figure 1

Receiver operating characteristic curve for discriminating between DID subjects and HCs. The dotted line indicates chance level and the solid line is constructed by varying the decision threshold smoothly between 0 and 1, plotting true positive rate (sensitivity) against false positive rate (1 – specificity). Points northwest of the dotted line indicate above chance discrimination. The area under the curve (AUC) summarises classifier performance across all decision thresholds.

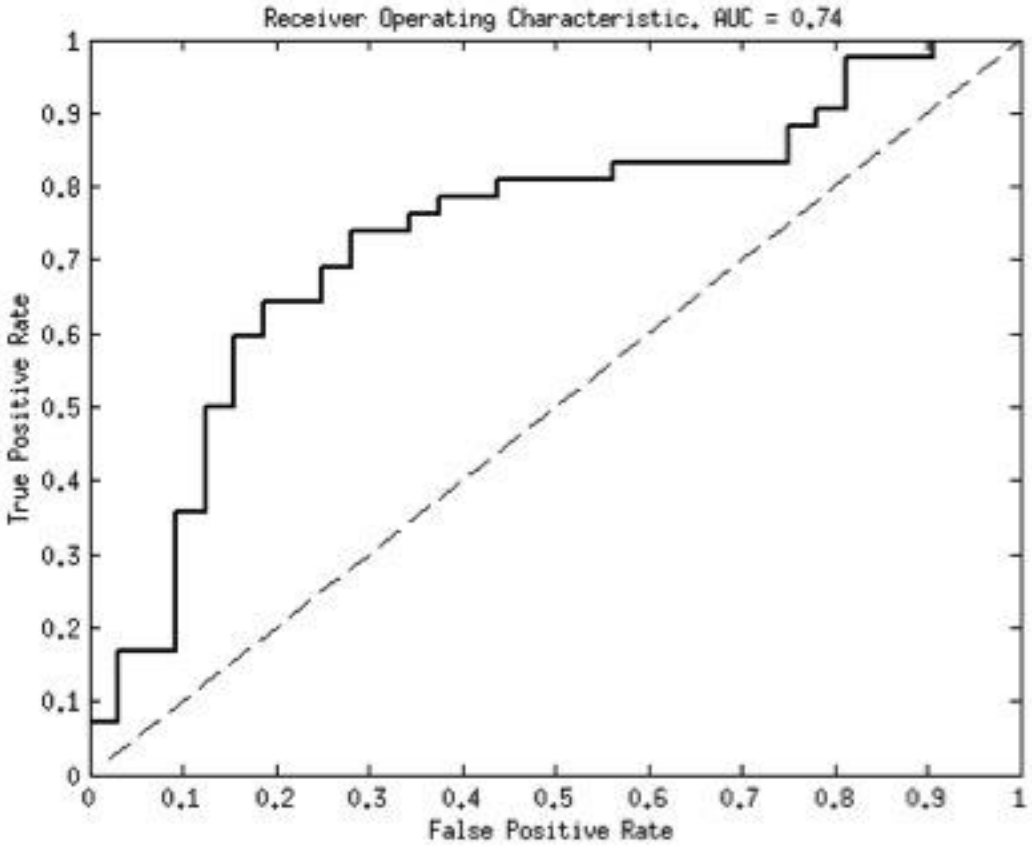


Figure 2

Forward map showing the underlying pattern of abnormality differentiating DID from normal healthy controls for grey (Figure 2A) and white (Figures 2B) matter. Coefficient images are overlaid on the study-specific anatomical templates in axial views. Images are scaled such that the maximum value in each image was equal to one, and only regions surviving the feature selection step are shown. Positive coefficients indicate a positive association in favour of DID, while negative coefficients indicate a positive association in favour of healthy controls.

Figure 2A: Grey matter, axial view

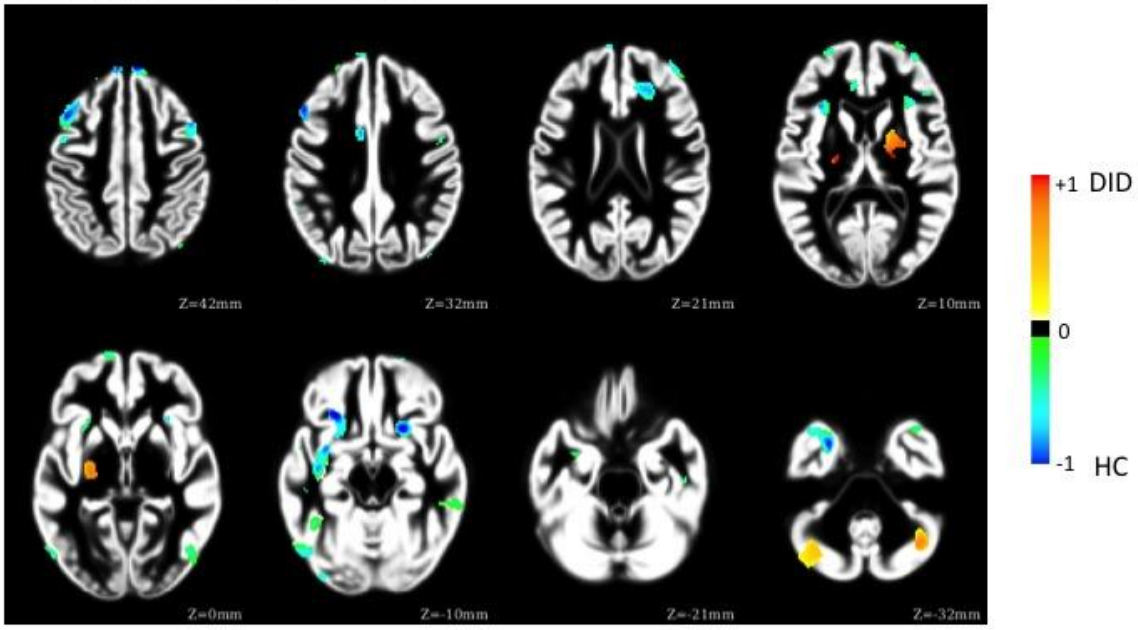
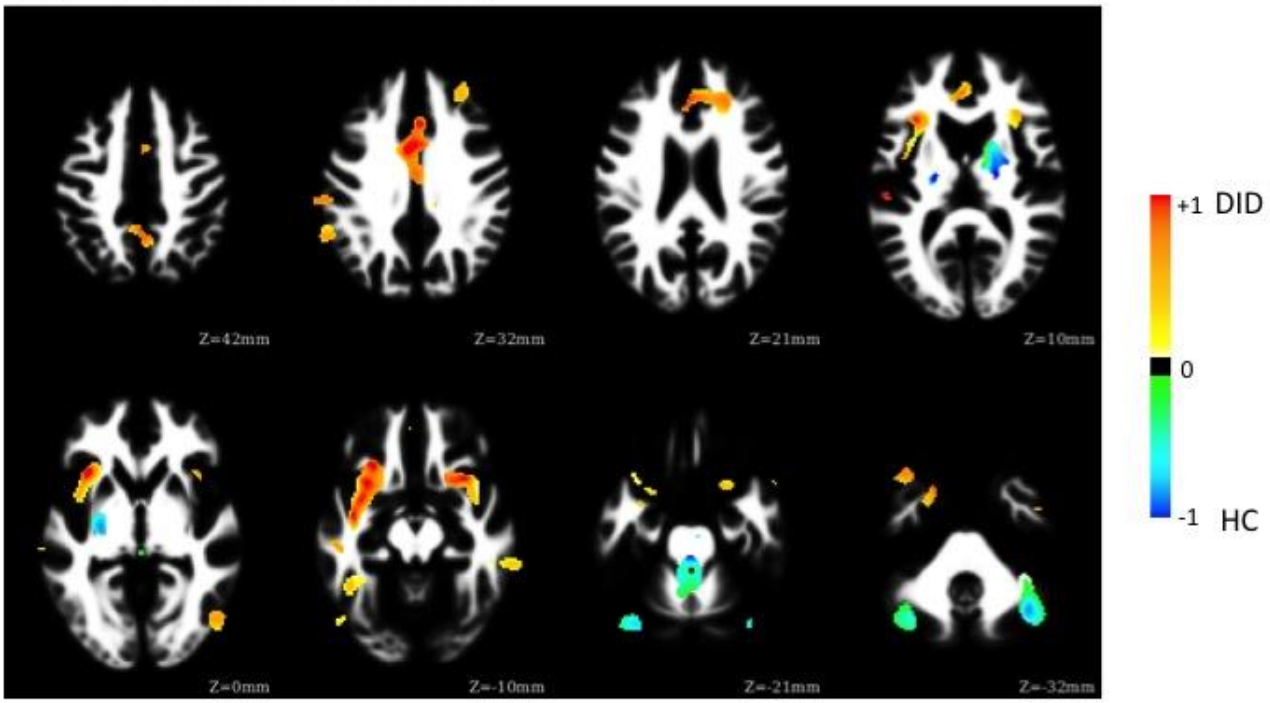


Figure 2B: White matter, axial view



SUPPLEMENTARY MATERIALS

Table presenting participant demographics

Supplementary Table 1: Participant demographics and clinical characteristics. These data have been previously reported in a similar manner.

	All		
	mean (std)		ttest
	DID-G (n=32)	HC (n=43)	p-value
Demographics			
Age	43.56 (9.34)	42.28 (11.57)	0.608
Education	14.31 (2.04)	14.84 (1.63)	0.220
Medication^			
anti-psychotics: n(typical,atypical)	(4,12)	0	NA
anti-epileptics: n	5	0	NA
anti-depressants: n	21	0	NA
Clinical measures			
Tramatic Experiences Checklist (TEC)			
emotional neglect	12.28 (2.58)	2.60 (4.39)	<0.001

emotional abuse	11.86 (3.26)	1.53 (3.23)	<0.001
physical abuse	11.69 (3.63)	0.60 (1.99)	<0.001
sexual harrasment	10.07 (4.29)	0.52 (1.57)	<0.001
sexual abuse	10.38 (4.41)	0.07 (0.34)	<0.001
total	18.45 (3.97)	3.14 (2.78)	<0.001
Dissociative symptoms			
psychoform (DES)	50.14 (17.94)	6.31 (5.07)	<0.001
somatoform (SDQ-20)	52.77 (16.32)	22.45 (2.41)	<0.001
Depersonalization symptoms (CDS)			
frequency	1.72 (0.67)	0.22 (0.16)	<0.001
duration	2.28 (1.11)	0.34 (0.35)	<0.001
total	117.47 (48.60)	16.60 (13.87)	<0.001

^ = past and present medication use

DES = Dissociation Experience Scale

SDQ-20 = Somatoform Dissociation Questionnaire

CDS = Cambridge Depersonalisation Scale